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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,458	10/13/2004	Ken Inose	TOYA114.004APC	3907

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EXAMINER

SHAW, AMANDA MARIE

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 09/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/511,458	Applicant(s) INOSE, KEN	
	Examiner Amanda M. Shaw	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 August 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This action is in response to the amendment filed August 11, 2006. Applicant's arguments have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn. This action is made final.

Claims 1-5 are currently pending. Claims 1-5 have been amended and will be addressed herein.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons set forth in the Office Action of 5/12/2006 and reiterated below.

Claims 1-4 are indefinite over the recitation of the phrase "the first probe and the second probe are annealed and the first probe and the target nucleic acid are annealed". This phrase is considered indefinite because it can be interpreted several ways. For instance it could mean that in a reaction tube containing multiple first and second probes and the target, that (i) some of the first and second probes hybridize to

each other and that some of the first probes hybridize to that target or (ii) that the first and second probes and the target all join together to form one hybridization complex.

RESPONSE TO ARGUMENTS

3. In the response filed August 11, 2006, Applicants amended the claims to clarify that the second probe has a second region that is complementary to at least a portion of the specific region of the first probe which is complementary to the target sequence.

This argument has been fully considered but is not persuasive. According to the claim language the first probe is capable of binding to the second probe and the target. The second probe is also capable of binding to the first probe and the target. Applicants argue that the second probe does not bind to the target. However there are no teachings in the specification or the claims which say that it cannot. It is noted that the second probe has two regions. The first region of the second probe is complementary to the non-specific region of the first probe and therefore the second probe is capable of binding to the first probe. The second region of the second probe is complementary to at least a portion of the specific region of the first probe which is complementary to the target sequence. It is noted that the portion of the second region of the second probe that is complementary to the first probe would not be able to bind to the target because it would have the same sequence as the target, however it is possible that a different portion of the second region of the second probe could bind to the target.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

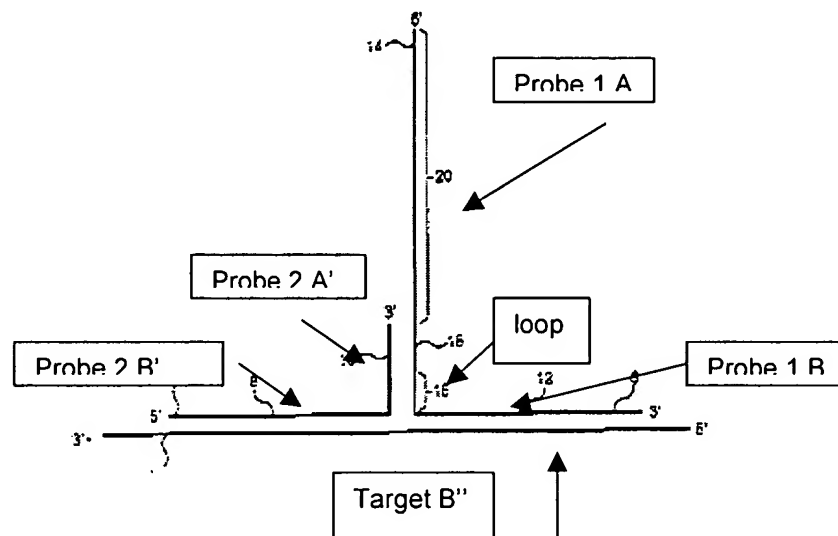
Claims 1, 3-5 remain rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Weston et al (US Patent 6391593 Filed 1999 and Issued 2002) for the reasons set forth in the Office Action of 5/12/2006 and reiterated below.

It is noted that Applicant cannot rely upon the foreign priority papers to overcome the 102(b) rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Weston et al teach a method for detecting a nucleic acid sequence using two hybridization probes. The first probe comprises a first region that is complementary to the target sequence (Probe 1 B) and a second region that is non complementary to the

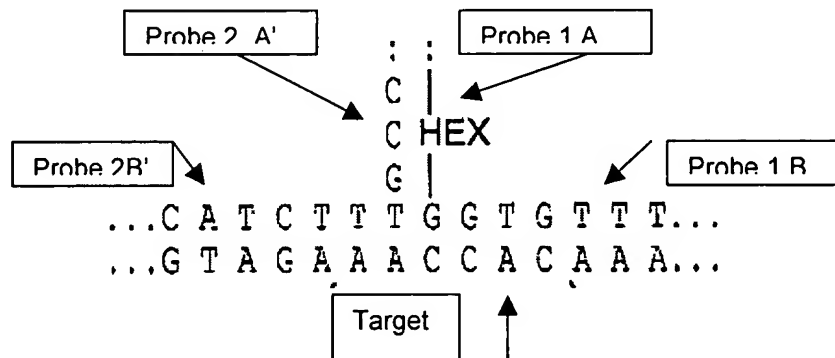
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target region (Probe 1 A). The second probe comprises a first region that has some complementary to the non complementary region of the first probe (Probe 2 A') and a second region that is complementary to at least a portion of the specific region of the first probe (Probe 2 B') (Abstract and See Diagram below).



According to Weston Probe 2 A' and Probe 1 A have between 5 and 15 bases that are complementary to each other and therefore these regions hybridize to each other. Additionally this region can comprise a destabilizing moiety (which produces a 2° structure such as a loop). According to this diagram the loop is on the first probe, however in other diagrams taught by Weston the loop is a property of the second probe (See Figure 11C). Weston teaches that the second region of the second probe is complementary to at least a portion of the specific region of the first probe. A schematic representation of this is shown in Figure 14B and below. Please take note that probe

2B' contains an "A" in the second position and a "C" in the fourth position. Probe 1B contains a "T" in the second position and a "G" in the fourth position. Thus these probes meet the requirement of the claim in that the second region of the second probe is complementary to at least a portion of the specific region of the first probe.



Additionally Weston teaches that these probes have detectable labels. In one embodiment the probes are fluorescence resonance energy transfer ("FRET") probes. FRET probes are probes in which a fluorescence signal may or may not be generated, depending on the conformation of the molecule. Typically, one part of the probe will comprise a fluorophore, and another part of the probe will comprise a "quencher" to quench fluorescence from the fluorophore. Thus, when the conformation of the probe is such that the fluorophore and quencher are in close proximity, there is no fluorescence, but when the fluorophore and the quencher are relatively widely separated, the probe does fluoresce (Column 10). Since the claim only states that "the nucleic acid is labeled" and does not specify which nucleic acid is labeled, for prior art purposes it does

not matter which probe is labeled (i.e. Probe 1 or Probe 2) or if the fluorophore is on one probe (i.e. Probe 1) and the quencher is on the other (i.e. Probe 2).

Regarding Claim 3, Weston et al teach that the labeling material comprises a fluorescent material and a quencher that quenches the fluorescence of the fluorescent material when the quencher is near the fluorescent material. Weston also teaches that the fluorescent material and the quencher may be arranged in a hairpin type (loop) structure (Column 10). Thus when the loop structure is present (when the first and second probes are bound) no signal is emitted, and when the loop structure is not present (when the first and second probes are not bound) a signal is emitted.

Regarding Claim 4, Weston et al teach that the method can be used to quantify the target nucleic acid (Example e 4).

Regarding Claim 5, Weston et al teach a kit for detecting the presence of a nucleic acid target sequence of interest. The kit comprises a pair of probes (such as those taught above) and appropriate packaging means. The kit may advantageously comprise one or more of the following: a DNA and/or an RNA polymerase, labeling reagents, nucleotide triphosphates (labeled or otherwise), detection reagents (e.g. enzymes, molecular beacons) and buffers (Column 7).

RESPONSE TO ARGUMENTS

5. In the response filed August 11, 2006, Applicants traversed the rejection over Weston. The arguments have been fully considered but are not persuasive.

The applicants first argue that the method of Weston requires that both the first probe and the second probe hybridize with the target while in the method of the

presently claimed invention the second probe only hybridizes with the first probe but does not hybridize with the target. However there are no teachings in the specification or the claims which teach that the second probe cannot hybridize with the target. In fact the claim language of "the first probe and the second probe are annealed and the first probe and the target nucleic acid are annealed" is so broad that it could be interpreted that in a reaction tube containing multiple first and second probes and the target, that (i) some of the first and second probes hybridize to each other and that some of the first probes hybridize to that target or (ii) that the first and second probes and the target all join together to form one hybridization complex.

The applicant further argue that in Weston the two probes do not hybridize to each other in the absence of the target while in the method of the presently claimed invention the two probes hybridize to each other in the absence of the target. The applicants state that regarding Figure 11 C it is noted that the probes 2B and 1B are complementary to each other in at least two bases but the applicants argue that these will not hybridize to each other as these probes are complementary only in two bases which are non contiguous. However there are no teachings in the specification of claims that say in order for two sequences to hybridize they must have at least N amount of complementary base pairs that are contiguous.

Additionally applicants argue that Weston et al teaches that the loop region forms only when the target is present and the two probes are annealed to the target while in the method of the present invention the two probes anneal to each other to form the loop. However Weston et al does in fact teach that the two probes anneal to each other

to form the loop. The only difference is that in the Weston reference the target is also present. The claims as written do not state that the target cannot be present when the loop forms.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 2 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Weston et al (US Patent 6391593 Filed 1999 and Issued 2002) for the reasons set forth in the Office Action of 5/12/2006 and reiterated below.

Weston et al teach that second region of the second probe is 10 or more bases long. Weston et al also teaches that the first region of the first probe is 10 or more bases long (Column 8).

Weston et al does not exemplify a method wherein the second region of the second probe is shorter than the specific region of the first probe.

However, the method of detecting target nucleic acids using hybridization probes of different lengths was well known in the art at the time the invention. Designing probes which are equivalents to those taught in the art is routine experimentation. The parameters and objectives involved in the selection of probes were well known in the art at the time the invention was made. Moreover, software programs were readily available

which aid in the identification of conserved and variable sequences and in the selection of optimum probes. The prior art is replete with guidance and information necessary to permit the ordinary artisan to design probes of different lengths which maintain their specificity. Thereby in the absence of evidence to the contrary, variants of the probes taught by Weston, including probes in which the second region of the second probe is shorter than the specific region of the first probe would have been obvious.

RESPONSE TO ARGUMENTS

7. In the response filed August 11, 2006, Applicants traversed the rejection over Weston. The arguments have been fully considered but are not persuasive. The applicants arguments over Weston have been presented above and addressed in paragraph 5.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

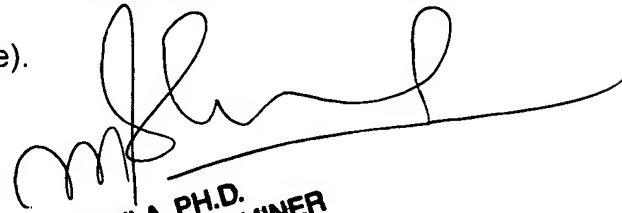
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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw
Examiner
Art Unit 1634



RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER